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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,521	09/14/2004	Jean Berthier	258409US0X PCT	6722

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EXAMINER
WILDER, CYNTHIA B

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
09/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/507,521	BERTHIER ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 5/4/2009 is acknowledged and has been entered. Claims 1-19 have been canceled. Claim 20 has been amended. Claims 20-38 are pending. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office action.

Previous Rejections

3. The prior art rejections under 35 USC 102(b) directed to claims 20, 22, 23, 25, 33 and 34 as being anticipated by Lockwood et al are maintained and discussed below. The prior art rejections under 35 USC 103(a) directed to claims 21, 24, 26-38 as being unpatentable over Lockwood et al in view of Lalchev et al in view of Ijiro et al are maintained and discussed below.

Claim Rejections - 35 USC § 102

4. Claims 20, 22, 23, 25, 33 and 34 are finally rejected under 35 U.S.C. 102(b) as being anticipated by Lockwood et al (Pharmaceutical Research, vol. 14, no. 11, 1997). Regarding claims 20, 22, 23, 25, 33 and 35, Lockward et al teach a method for concentration of a macromolecule in a liquid sample, the method comprising: providing a liquid medium, the liquid medium comprising the liquid sample and an interface layer,

wherein the interface layer located on the surface of the liquid sample, fixes the macromolecule and has a small volume as compared to liquid sample, forming a stabilized dispersion form by injection directly in the liquid sample of gaseous streams to form an interstitial medium constituting the foam; and resorbing the dispersion to reform the interface layer by drainage of the interstitial medium constituting the foam , wherein the macromolecule is enriched or concentrated in the interface layer which is collected as the foamate (see entire reference, such as e.g., abstract and sections entitled "The Foam Fractionation process" at pages 1511 and 11512 and "solution conditions and operational parameters at page 1513). Lockwood teaches wherein the macromolecule is protein (abstract) and wherein the method allows for enrichment, purification and detection (see pages 1512 and 1513). Therefore, Lockwood et al meet the limitations of the claims above.

Claim Rejections - 35 USC § 103

5. Claims 21, 24, 26-38 are finally rejected under 35 U.S.C. 103(a) as being unpatentable Lockwood et al (Pharmaceutical Research, vol. 14, no. 11, 1997) and Lalchev et al (Biotechnology and Bioengineering, vol. XXIV, pages 2253-2262, 1982) in view of Ijiro et al (citation made of record). Regarding claims 24, 26, 27-28, Lockwood et al teach a method for enriching a macromolecule in a liquid sample, the method comprising: providing a liquid medium, the liquid medium comprising the liquid sample and an interface layer, wherein the interface layer located on the surface of the liquid sample, fixes the macromolecule and inherently has a small volume as compared to liquid sample, forming a stabilized dispersion form by injection, directly in the liquid

sample of gaseous streams to form an interstitial medium constituting the foam; and resorbing the dispersion to reform the interface layer by drainage of the interstitial medium constituting the foam , wherein the macromolecule is enriched or concentrated in the interface layer which is collected as the foamate (see pages 15111-1513). Lockwood et al teaches wherein the macromolecule is protein, which inherently encompasses the teaching of prions, which are protein molecules (e.g., abstract).

Lockwood et al do not teach wherein the macromolecule is DNA.

Lockwood et al however teaches that the method of foam fractionation can be used to separate DNA and protein (see bottom of page 1512, col. 2 bridging page 1513, col. 1). Lockwood cites Lalchev et al to support this assertion. Lalchev et al teach the successful use of foam fractionation to separate DNA and protein (see e.g., abstract and pages 2254 and 2255).

Lockwood in view of Lalchev et al do not teach wherein the method comprises specific means of fixing the macromolecule as required in the claims.

Ijiro et al. teach a method comprising forming a stabilized dispersion of an emulsion type from a medium comprising said liquid sample and an interface layer,, wherein said interface is a gas-liquid interface, such as taught by Lockwood et al, said interface layer capable of fixing macromolecules (col. 2, lines 46-60; col. 3, line 35 to col. 4, line 61). Ijiro teaches wherein the fixing of the macromolecule is by chemical affinity ((col. 2, lines 46-60; col. 3, line 35 to col. 4, line 61). Ijiro et al teaches wherein the macromolecule is DNA (col. 3, lines 55-56). Likewise, Ijiro et al teaches wherein the macromolecule is DNA and the molecule capable of fixing the DNA is functionalized

with a probe to allow specific hybridization of the DNA or an intercalator (col. 3, line 54 to col. 4, line 13).

In view of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention that one of ordinary skill in the art could obtain predictable results of enriching DNA or protein using the known methods of foam/emulsion fractionation as taught by Lockwood et al in view of Lalchev et al and Ijiro et al. On of ordinary skill in the art at the time of the claimed invention would have been motivated to utilize foam/emulsion fractionation for the purpose of enriching nucleic acids or proteins or collidal particles based on the advantages taught by Lockwood that foam fractionation has the potential to be a cost-effective component of purification/enrichment schemes (see abstract).

With regards to the claims 21, 29-32, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization of reaction components, concentrations, and parameters as evidence by Ijiro et al. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. Thus, one of ordinary skill in the art at the time of the claimed invention would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations an/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods using different means of mixing and fixing the DNA as claimed for the obvious benefit of detecting specific hybridization or for the benefit of controlling or detecting the

orientation of the nucleic acid as taught by Ijiro et al (col. 7). The combination of Lockwood et al in view of Lalchev et al and Ijiro et al is *prima facie* obvious in the absence of secondary consideration.

Regarding claims 35-38, Lockwood et al in view of Lalchev et al and further in view of Ijiro et al teach a method of enrichment/purification of a macromolecule, wherein the macromolecule is DNA or protein. Ijiro et al teach wherein the DNA is further used in hybridization reactions. The references do not teach wherein the DNA (macromolecule) is used in amplification reaction. However, it would have *prima facie* obvious to the ordinary artisan at the time of the claimed invention that the enriched or purified DNA or protein could be used in any of the plethora of well known biochemical reactions, such as nucleic acid amplification, sequencing, hybridization and etc. As noted earlier, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization or reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations an/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods in the absence of secondary consideration.

Response to Arguments

6. Applicant traverses the rejections on the following grounds: Applicant summarizes the instant invention and then summarizes the teachings of Lockwood et al. Applicant asserts that the Lockwood fails to provide an interface layer, where the interface layer is located at the surface of the liquid sample, fixes the macromolecule or the agglomerate and has a small volume compared to the volume of the liquid sample. Applicant states that the in Lockwood et al, nitrogen is bubbled directly into the sample solution. Applicant states that since Lockwood fails to provide an interface layer, the reference necessarily fails to disclose resorbing the dispersion to reform the interface layer by drainage of the insterstitial film constituting the foam or by drainage of the interstitial medium constituting the emulsion, where the macromolecule or the agglomerate is concentrated in the interface layer, as claimed.

With regards to the rejections under 35 USC 103, Applicant states that Lockwood fails to provide an interface layer as discussed earlier. Applicant further states that Lalchev et al to fails to disclose an interface layer and that Ijiro neither discloses nor suggests forming a stabilized dispersion followed by a resorption step as claimed.

7. All of the arguments have been thoroughly reviewed and considered but are not found persuasive. In response to Applicant's arguments that the reference of Lockwood et al fails to provide an interface layer, the Examiner respectfully disagrees. Firstly, the Federal Circuit discussed claim interpretation by the PTO in *In re Morris*, where the Federal Circuit noted "[A]s an initial matter, the PTO applies to the verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account

whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 44 USPQ2d 1023, 1029 (Fed. Cir. 1997). The decision of the court in *In re Bigio*, 72 USPQ2d 1209 (Fed. Cir. 2004) strongly supports the breadth of interpretation. That court noted "[T]his court counsels the PTO to avoid the temptation to limit broad claim terms solely on the basis of specification passages." In concert with *Morris* and *Bigio* is the decision in *In re American Academy of Science Tech Center*, 70 USPQ2d 1827, 1834 (Fed. Cir. 2004), where the Federal Circuit noted "We have cautioned against reading limitations into a claim from the preferred embodiment described in the specification, even if it is the only embodiment described, absent clear disclaimer in the specification."

In this case, the specification at the bottom of page 6 bridging top of page 7 defines "interface layer" as a "monolayer (or virtually two-dimensional zone) located at the surface of the liquid sample (referred to as first liquid phase) comprising the macromolecule or the agglomerate to be concentrated. This layer, by virtue of its nature and specific properties, is able to provide the selective transfer of the macromolecule or of the agglomerate from the liquid sample to the interface layer and due to its tiny volume compared to the liquid sample, of concentrating aid macromolecule or said agglomerate". Lockwood et al meets the limitations of the claims as currently written. Lockwood et al teach at page 1512, "there are two modes of operation by which foam fractionation may purify a protein, the difference lying in the relative-surface activities between the contaminates and the protein of interest". Lockwood teaches if the contaminants are more surface active, they will be removed via the foam, leaving he

product in the residual solution. On the other hand, if the product of interest is more surface active, it will be enriched in the foam. Upon creation of a surface, the initial population of molecules at the interface is governed by a complex interaction of factors such as concentration, diffusivity, molecular flexibility and hydrophobicity. Lockwood teaches that due to high molecule weight, proteins are slow to absorb, typically exhibiting diffusion control. Lockwood states that the affinity of a protein for the surface tend to be high as a result of the summed interaction of many hydrophobic force-driven points of attachment to the interface. Lockwood additionally depicts wherein the foamate is collected from the surface of the foam comprising the macromolecule of interest (Figure 1 and 2). Thus, the Examiner maintains that the Lockwood teaches the claims as currently written. Applicant is additionally reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The rejections under 35 103(a) as being unpatentable over Lockwood et al in view of Lalchev et al in view of Ijiro et al is maintained for the same reasons discussed above. Applicant's arguments are not sufficient to overcome the rejections of the prior Office action.

Conclusion

8. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637